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CONTRIBUTIONS FROM THE ZOÖLOGICAL LABORATORY OF THE MUSEUM OF COMPARATIVE ZOÖLOGY AT HARVARD COLLEGE. E. L. MARK, DIRECTOR. — No. 142.

THE HEREDITY OF ALBINISM.

BY W. E. CASTLE AND GLOVER M. ALLEN.

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I. Introduction.

This paper contains a preliminary statement of certain results of breeding experiments with mice, guinea-pigs, and rabbits, which have been conducted in the Zoölogical Laboratory of Harvard University during the last two and a half years. The experiments with mice are the work principally of the junior author; those with guinea-pigs and rabbits, of the senior author.

Albinism, or absence of the normal pigmentation of an organism, is a not infrequent phenomenon in both animals and plants, yet its occurrence in nature is sporadic and has usually been interpreted as an indication of organic weakness. But this interpretation is probably erroneous, for albino races of domesticated animals are apparently not inferior in vigor to other races. Such is demonstrably the case with albino mice.

The idea that albinos lack constitutional vigor may have its origin in the observation that, in crosses between albinos and normal individuals,

no albino offspring are produced. But the disappearance of albinism in this case is not final. The albino character has not ceased to exist, but has merely become latent in the offspring. It will reappear unimpaired in the next generation if the cross-bred individuals be mated *inter se*.

II. Complete Albinism a Recessive Character.

The disappearance of the albino character for a generation, and its subsequent reappearance under close breeding, show that it is inherited in conformity with Mendel's law of heredity,* and that it is, in the terminology of that law, a *recessive* character.

(*a*) *In Mice.*

In mice this has been conclusively demonstrated by Cuénot (:02),† who, on crossing wild gray house-mice with albinos, obtained always gray mice indistinguishable in appearance from the pigmented parent. Yet these gray hybrids, when bred *inter se*, produced both gray and white offspring approximately in the Mendelian ratio, 3 : 1. The exact numbers recorded are 198 gray: 72 white, or 26.6 per cent albinos. According to Mendelian principles the grays of this second filial generation should consist in part of *pure* grays, which would not transmit the albino character, and in part of *hybrid* grays like their parents, — the first filial generation, — which would transmit alike the pigmented and the albino characters. This Cuénot demonstrated to be actually so, for certain pairs formed by random selection of the grays gave only gray offspring (189 individuals); the remaining pairs produced albino as well as gray offspring, and in the expected ratio, 3 grays : 1 albino.

* A brief statement of Mendel's law has been made by one of us elsewhere (Castle, :03[a]). For a fuller exposition, see Bateson (:02), Bateson and Saunders (:02), de Vries (:02), or Correns (:01).

† In an earlier paper (Castle, :03[a]) the first published recognition of the recessive nature of albinism in mice is erroneously credited to Bateson (:02). The papers of Cuénot (:02, :02[a]), which at that time were unknown to us, apparently antedate Bateson's.

Crampe ('85) seems to have been the first to recognize clearly that the first cross between pigmented and unpigmented (albino) varieties gives rise, in the case of rats, to pigmented individuals, *not* to albinos. Crampe crossed gray, black, gray-white, and black rats (*Mus norvegicus*) with albinos, and found that in each cross the albino character disappeared. He noticed also that the albino character might reappear in subsequent generations, but he did not discover the conditions necessary for this reappearance beyond establishing that albino offspring were produced under close breeding by those pigmented rats only in whose immediate ancestry there had been a cross with the albino form.

The precise numbers recorded are 162 grays: 57 albinos, or 26 per cent albinos.

Cuénot's observations are fully substantiated by experiments performed by the junior author of this paper, a full account of which will be published elsewhere. Wild gray mice were crossed with albino mice, and the offspring, sixty-four in number, were all gray like the wild parent, though a single litter of three young, which died without attaining their full growth, were of a somewhat lighter gray than the wild parent. Certain of the cross-breds were paired together, and produced 66 offspring, 42 of which were gray, 24 white. This is a considerable deviation from the expected ratio, 3 : 1, but it should be remembered that the total number is relatively small. The result is of the *nature* expected, in that both gray and albino offspring are produced, and of the former a larger number than of the latter.

To determine whether the grays are, as expected, of two sorts, one hybrid, the other pure, six pigmented individuals have been crossed with the parental white stock. Three of the six have thus far produced only pigmented offspring, indicating that they are pure; the other three have produced both gray offspring and white offspring, showing that they are hybrids. The two sorts of offspring produced in the case last mentioned should, according to Mendelian expectation, be equally numerous.

The numbers thus far recorded are 35 pigmented individuals: 23 albinos, a result agreeing with expectation in that both gray and white offspring are produced, though these are not in the exact proportions demanded by Mendel's laws.

If we *combine* the results of this cross with those obtained by interbreeding hybrids of the first filial generation, we get for the whole a close agreement between expectation and observation. The expectation is 78.5 gray : 45.5 white; the observed result is 77 gray : 47 white.

White mice obtained by one or the other of these crosses have repeatedly been bred together, but without the occurrence of a single exception to the expected Mendelian result, the offspring being invariably albinos.

A further test of the Mendelian hypothesis as applied to albinism in mice was made by Cuénot. By back-crossing hybrid grays with the ancestral white stock he obtained gray as well as white individuals, which in the phraseology of breeders should be $\frac{1}{2}$, $\frac{3}{4}$, $\frac{7}{8}$, etc., white "blood," yet all the grays, irrespective of ancestry, gave precisely similar results in crosses with whites, viz. equal numbers of gray and white offspring.

It is evident, then, that when a pure gray race of mice is crossed with a pure white race, the gray character invariably dominates in the off-

spring, and in subsequent generations both gray individuals and white individuals occur approximately in the proportions demanded by Mendel's principles of dominance and segregation. No better illustration of Mendel's law has yet been produced than is afforded by the cross between gray and white mice.

(*b*) *In Other Mammals, in Fishes, and in Plants.*

In the case of guinea-pigs, we have many times mated together albinos born of mottled parents, or obtained by mating a mottled with a white animal, but never with any but the expected Mendelian result, all the young being albinos.

In the case of rabbits, the same law appears to hold. Professor R. T. Jackson kindly placed at our disposal last summer three white rabbits, a male and two females, all born in the same litter, of spotted parentage. The two females have borne by their brother, in three litters, seventeen young, all albinos.

In man, Farrabee (:**03**) and Castle (:**03**) have recently shown albinism to be in all probability recessive.

As to fishes, Dr. Hugh M. Smith, of the United States Fish Commission, informs us that in one of the State fish-hatcheries of this country there is bred as a curiosity a race of albino trout which "*breed true*," indicating that the albino character is recessive.

In plants, more than two-thirds of the Mendelian cases mentioned by de Vries (:**02**, p. 146) are cases of "depigmentation" of flowers or fruit, the depigmented condition being invariably recessive in crosses with the normal condition.

It appears, then, that in organisms in general, albinism behaves as a recessive character in heredity.*

III. Partial Albinism a Mosaic of Dominant and Recessive Characters, and a Unit in Heredity.

Darbishire (:**02**) finds that in crosses between a peculiar race of partial albino mice and true albinos, the albinism does not entirely disappear in the offspring, and he thinks that this weighs heavily against the entire

* The only exception known to the writers is the dominance of white plumage, in certain crosses of poultry, as recorded by Bateson and Saunders (: **02**). Yet the dominant character in this case is one of *partial* albinism only, and its dominance is not invariable. We suspect that the dominance of white plumage results from its *coupling* in the gametes with some other character strongly dominant by nature.

Mendelian hypothesis. In reality Darbishire's observations, when rightly interpreted, afford strong evidence in favor of that hypothesis. It may be well, therefore, to examine them with some care. But before doing so one or two earlier observations should be noticed.

Haacke ('95) crossed spotted blue-[black-]and-white Japanese dancing mice with albino mice, and obtained offspring uniformly gray in color, like the wild house-mouse, or uniformly black. Occasionally, however, one of the gray or black offspring bore a fleck of white on forehead or belly.

Von Guaita ('98, :00) repeated the experiment, crossing spotted black-and-white Japanese dancing mice with an inbred stock of albinos. He obtained twenty-eight young, all uniformly gray like the house-mouse. These gray mice bred *inter se* yielded in subsequent generations gray, gray-white, black, black-white, and white offspring.

Darbishire's experiment consisted in crossing albino mice with a peculiar race of Japanese dancing mice which had *pink eyes* and were uniformly white except for patches of pale fawn-color on the cheeks, shoulders, and rump. The dancing mice had been tested and found to breed true *inter se.* From the cross between these partial albinos and true albinos forty-eight young were obtained, of which all except two were marked more or less extensively with *gray;* those two were *fawn-color all over* except on the belly, where — we infer from Darbishire's likening them to certain of his gray mice — they were either of a *lighter* fawn-color or else white.

Of the forty-six young which were marked with gray, fifteen were gray all over except on the belly and tail, where they are said to have been "nearly white." What is meant by this expression we do not know, unless it be a light shade of gray. If this is the author's meaning, then the fifteen mice were really gray all over. The wild house-mouse itself is often lighter colored on the belly and tail, and these fifteen individuals must be regarded as substantially complete reversions to the gray pigmented type of the wild house-mouse, a type radically different from that of either parent. This result agrees with that obtained by Haacke ('95), von Guaita ('98, :00), and ourselves, upon crossing spotted with albino mice. In thirteen of the forty-six gray-marked mice obtained by Darbishire, the gray covered much more of the body than did the fawn in the Japanese parent; while in eighteen others the gray corresponded roughly in distribution with that of fawn in the Japanese parent. In no case is the gray described as being less extensive than the fawn in the Japanese parent, and *no mention is made of any hybrid*

having pink eyes, though both parents had unpigmented eyes.* Not only were the offspring *not intermediate* in pigmentation between the two parents, as we should expect on any hypothesis other than the Mendelian one, but *not a single mouse in the forty-eight contained as little pigment as was found in the pigmented parent.* In every case the pigmentation was greatly increased over what it had been in the pigmented parent, either in intensity or in extent, and usually in *both* respects. *Not a single albino was produced*, though the mother had been in every case an albino. Yet Darbishire maintains that the case is not one of Mendelian dominance!

It is hard to imagine a plainer case of Mendelian dominance than this, — a spotted mouse is bred to a white mouse; the offspring are all spotted, none white. The spotted character is plainly dominant, the white, recessive! What would Darbishire require to satisfy him that the case is a Mendelian one? Offspring all like *neither* parent, but like a third form, a supposed ancestral form. But is this simple dominance? No, it is dominance associated with something else, reversion, i. e., the coming again into activity of a character long latent, in this case the formation of black pigment. Because the *reversion* is not in every case complete, Darbishire maintains there is no *dominance*, a conclusion utterly fallacious.

What is the true explanation of cases of heredity like that observed by Darbishire? The explanation has been given elsewhere by one of us (Castle, :03[a]), but it may be well to repeat it here. Albinism is in mice and other mammals a character recessive in relation to the pigmented condition. But the spotted mouse is not a simple dominant (pigmented) individual as contrasted with simple recessive (albino) individuals. The spotted mouse is a peculiar kind of individual, in which are found both the dominant and the recessive characters, yet not in their usual relationship (one latent, the other alone visible), but *both* visible side by side, in distinct areas of the animal's body. Such an individual is called a *mosaic*. In the soma of a mosaic individual the law of dominance is suspended, but cross-breeding serves usually to bring it again into operation in the next generation, for the crossing of a mosaic with a normal, or with a recessive individual, results usually in the production of normally pigmented individuals only. Thus when spotted rats or mice are crossed either with gray individuals (dominants) or with albinos (reces-

* This significant omission was observed by Bateson also, who mentions it in a letter received since the above paragraph was written.

sives), the offspring are commonly all gray or black in color, none spotted. Here we find that dominant and recessive characters have abandoned the balanced relationship which they had in the spotted parent, and returned to the ordinary relationship of a dominant to a recessive character.

Just as in mosaic individuals the law of dominance is suspended, so, too, in the formation of their gametes the law of segregation is commonly suspended also. The gametes, as well as the soma, of a mosaic individual are commonly mosaic, containing side by side the dominant and the recessive characters. For it is evident from the experiments of Haacke, von Guaita, and Darbishire that the spotted mice employed by them in crosses with albino mice did not form any gametes containing *only* the recessive (albino) character, otherwise albino offspring would have been produced, but *not one* was produced. Hence segregation of the pigment-forming character from the albino character cannot have occurred at the formation of gametes in these several cases, but the gametes themselves must have possessed a mosaic (or else a dominant) character.

A similar explanation must be made of certain results obtained by one of us in crossing black-white (not dancing) mice with albino mice. Two spotted males of a black-white stock which bred true *inter se*, were crossed with albinos. The offspring were like those obtained by Haacke in crossing Japanese dancing mice with albinos, namely, mice uniformly gray or black in color, though sometimes with a fleck of white on the belly, or with one or more white bands on the tail. Of the forty-three young produced by this cross, twenty-eight were gray, and fifteen black. The fact that no albino offspring were produced shows that the spotted males formed no recessive gametes, but only those which were either mosaic, or else purely dominant, in character. But if dominant gametes had been formed by segregation from a dominant-recessive mosaic, we should expect that by a residual process *recessive* gametes would be formed also. The latter not having been formed, it is safe to suppose that the former were not formed either, but that *all* the gametes formed by these spotted males were *mosaic*.

That the albino character entered as a latent constituent into the gray or black hybrids formed by the cross just described, is shown conclusively by the character of their offspring. When bred *inter se* they produced albino as well as pigmented offspring, and approximately in the ratio, 1 : 3; or, when bred to albinos, in the ratio, 1 : 1.

Accordingly, in the original cross described, we have a case of simple

dominance of the pigment-forming over the albino character. This dominance is attended, in about two cases out of three, by reversion to the particular form of pigmentation found in the wild house-mouse. The reversion is due to the coming into activity of a capacity (previously latent) to form *yellow* pigment, which with black pigment forms gray. This latent capacity must have been present in one or the other or possibly in *both* of the parents crossed.

Darbishire's results differ from ours only in degree, not in kind. He, too, gets invariably dominance of the pigment-forming over the albino character, and this is associated in all except two out of forty-eight cases with reversion to the ancestral *kind* of pigmentation, gray. The only differences between his results and our own are as follows: —

1. In our experiments *yellow* was the latent constituent of gray which was brought into activity by a cross with albinos; in the experiments of Darbishire *black* was the latent constituent brought into activity.

2. In our experiments white disappeared for the most part from the bodies of the hybrids; but in Darbishire's experiments the disappearance of white was much less complete. There was a strong tendency for the mosaic gamete to *dominate as a unit* without serious disturbance of the balanced relationship of pigmented and unpigmented areas in the mosaic structure. This tendency is observable in thirty-one out of forty-eight cases. The remaining seventeen cases are strictly comparable with our own. In fifteen of them the black character, latent in one or possibly in both parents, has become active and, combining with yellow (fawn), visible in one parent, has formed gray; in the other two offspring, black, if present, has remained latent, leaving the individuals fawn-colored. This result is comparable with the production of *black* hybrids in our own experiments.

In Darbishire's experiments, as in our own, the effect of a cross with albinos is to release the dominant character from the strict localization which it had in the mosaic parent. In Darbishire's mosaic mice the localization of pigment was much more rigid than in our own. His mice bore pigment only on the shoulders and rump, and had *pink* eyes; ours were pigmented over at least half of the body and had *black* eyes. It is not surprising, then, that the pigmentation should be less extensive in Darbishire's hybrid mice than in our own. Yet it is evident that in all his hybrids there occurred release, more or less complete, of the pigment-forming character from its localization in the original mosaic. In every case, apparently, the hybrid had pigmented eyes, though neither parent possessed this character.

IV. Pure and Hybrid Mosaics.

In our experiments in crossing spotted with albino mice, a third black-white male was employed. He was a half-brother * to the two spotted males previously mentioned, born of the same mother but by a different sire. The white areas on his body were less extensive than those on his two brothers. He was bred to the same stock of white females as they, but with different results. By him the albinos bore albino as well as pigmented offspring; of the former twenty-one, of the latter twelve, ten being gray and two black. The albino offspring were found in this case, as in all others tested, to breed true *inter se*.

It is evident that the third black-white male differed in nature from his two half-brothers, for he formed *recessive* gametes, whereas they did not.

Examination of other breeding records of spotted mice kept by us during the past two years shows that it is possible in these also to distinguish two different sorts of mosaic individuals. These are: —

1. *Pure mosaics*, spotted and forming only mosaic gametes, *DR*. They bred true *inter se*, but when crossed with albinos produce only individuals of the following class.

2. *Hybrid mosaics*, usually *more extensively pigmented than pure mosaics*, often pigmented all over. (Compare the results of Haacke, von Guaita, and Darbishire.) They form, in approximately equal numbers, mosaic and recessive gametes, $D\,R$ and R respectively. Accordingly, when bred *inter se*, they produce offspring of three different sorts, $D\,R$, $D\,R\cdot(R)$ [or $D(R)\cdot(R)$],† and R, that is, pure mosaics, hybrid mosaics, and recessives. Theoretically these three classes of offspring should be numerically as 1 : 2 : 1. There is reason to believe that these proportions are approximated in our experiments, but this matter has not yet been fully tested. When bred to albinos, hybrid mosaics produce (in equal numbers?) hybrid mosaic and albino offspring.

It is possible to recognize in the experiments of von Guaita also these two different classes of mosaics. Von Guaita's original stock of dancing mice consisted of *pure* mosaics, for they bred true *inter se* and when bred

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* In an earlier paper (Castle, : 03 , p. 542) it is stated erroneously that this mouse was an *own* brother to the other two.

† The period is used to indicate the distinctness, in the zygote, of the gametes which united to form that zygote, as well as to show that, when in the hybrid individual segregation of characters takes place at gamete formation, splitting will occur at the point marked by the period, producing gametes *DR* and *R*.

to albinos produced only pigmented offspring. These offspring, though not themselves spotted, were clearly *hybrid mosaics*, for when bred *inter se* they produced spotted as well as albino offspring, of the former nine, of the latter fourteen, in a total of forty-four young; the expectation on our hypothesis is eleven of each!

The idea that there are, as just explained, two different sorts of mosaic individuals, originated with the junior author of this paper. It constitutes a discovery of no small importance, one which lends strong support to the Mendelian hypothesis of essential gametic purity. It shows that alternative parental characters, when united in fertilization, do not mix, but that each retains its own identity and subsequently separates from the other when gametes are formed. This takes place *even when one of the parental characters is itself a mosaic!* Herein we have a confirmation of the conclusion based upon morphological observations, that the paternal and maternal contributions to the zygote retain each a distinct individuality. Further, the idea of Bateson receives confirmation, that the gray color of mice obtained by crossing black-white with white mice is itself a "heterozygote" character.

Darbishire's premature conclusion, that in his spotted hybrids "albinism is not recessive," will undoubtedly be abandoned by him when he has reared from them a second generation of hybrids. From our own experiments and those of von Guaita we confidently predict that he will obtain approximately one in four of albino mice, and of the pigmented mice obtained, part will be *pure mosaics* (as defined by us), but a larger part will be *hybrid mosaics* like their parents.*

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* This prediction has been fulfilled sooner than we had expected. In a paper just received Darbishire (:03) states that his hybrid mice bred *inter se* have produced 66 young. Of these 13 are albinos, and 17 are (in our terminology) pink-eyed mosaics, while the remaining 36 have dark eyes. The last named class consists clearly of *hybrid* mosaics like their parents. The Mendelian expectation is that half the offspring, or 33, will be of this sort; the observed number is 36. The other two classes (albinos and pure mosaics) should theoretically number 16.5 each, or together 33; they number 13 and 17 respectively, or together 30.

The correctness of this interpretation of Darbishire's results can easily be tested by further breeding of his animals. The pink-eyed individuals, if really pure mosaics, as we suppose, will, when bred to albino individuals, produce only dark-eyed offspring; whereas their dark-eyed brothers and sisters when similarly mated will produce both dark-eyed individuals (like themselves) and albinos, in approximately equal numbers. Further, the pink-eyed individuals will probably breed true *inter se*, whereas dark-eyed individuals will continue to produce in subsequent generations, as in the case already observed by Darbishire, offspring of three sorts,

V. Pure and Impure Recessives.

Although Darbishire's interpretation of his results is clearly unsound, he has made an observation of great importance, both theoretical and practical. In his crosses with dancing mice, he employed two different stocks of white mice, and with results somewhat different in the two cases. The two stocks were (1) "pure-bred" albinos purchased from breeders, and presumably descended from white parents, and (2) "cross-bred" albinos known to be descended from spotted [i. e. hybrid mosaic] parents. The latter, when crossed (four different pairs) with the fawn-white dancing mice, produced only spotted gray-white offspring, nineteen in number. The former, when crossed in the same manner (five different pairs), also produced gray-white mice, twelve in number, but produced in addition fifteen gray mice (with lighter bellies and tail) and two

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namely, albinos, dark-eyed individuals, and pink-eyed individuals, approximately in the proportions, 1 : 2 : 1.

The numbers of first- and second-generation hybrids which have been reared by Darbishire are now considerable. They show conclusively that both albinism and the dancing character are recessive in relation to the normal conditions. The original cross between pink-eyed dancing mice and albinos has yielded 203 offspring, all dark-eyed and with bodies more or less extensively pigmented; none dance. Certain of these hybrids bred to albinos have produced 205 young, of which 111 are albinos; the Mendelian expectation in this case is 102.5 albinos. The remaining (pigmented) offspring of this cross are all dark-eyed like their hybrid parent, and none dance; this is precisely the Mendelian expectation.

First-generation hybrids bred *inter se* have yielded both albinos and dancing individuals. The Mendelian expectation is one in four of either sort. The observed number of albinos is, as already stated, 13 in a total of 66; the number of dancers in the entire 66 is not stated, but we are told that, in 37 mice of this generation, 8 were dancers; the Mendelian expectation is 9.

Darbishire grants that these facts are "in possible accordance with some form of Mendelian hypothesis," but holds that "the behavior of eye-color is in every respect discordant with Mendel's results." The latter conclusion he reaches only by first assuming that "the possession of pink eyes must on Mendel's view depend on a separate embryonic element from that which determines coat-color." This is a wholly unnecessary assumption. The pigmented areas of the eye are morphologically and (as far as heredity is concerned) also physiologically parts of the general integument. A pink eye is simply an eye devoid of pigment; it represents an unpigmented area of the integument, and is no more a distinct element in heredity than is an unpigmented (white) spot on the side or tail of the animal. In an earlier paper (Castle, : **03**[a], p. 543) one of us has likened a white animal with dark eyes to a white animal with dark extremities, both are essentially mosaics of the dominant and recessive characters. On this view the observed inheritance of eye-color is in every respect *accordant* with Mendel's results.

fawn-colored mice (likewise lighter below). The two fawn-colored mice were borne by a single "pure-bred" mother. Gray mice were borne by all five "pure-bred" mothers.

This result indicates that *not all albinos breed alike* when crossed with the same pigmented stock, a conclusion which our own experiments fully substantiate. Darbishire's white mice clearly show individual differences in the way in which they breed. These differences are even more striking among the "pure-bred" than among the "cross-bred" mothers, doubtless because the former were obtained from different breeders, whereas the latter all came from one source.

Darbishire is entirely right in concluding that the ancestry of white mice does "make a difference" in their breeding capacity, but he is certainly wrong when he surmises that "the more in-bred an albino is the less power it has of transmitting its whiteness," unless he is willing to limit this statement to the *first hybrid* generation, which, however, he has not done. The truth probably is that in crosses between albino and spotted races, *reversion* to the ancestral form of pigmentation is more complete the *purer* the white stock is. But the ability of the white parent to transmit its whiteness to generations other than the first is certainly not diminished by inbreeding. For, while von Guaita employed a stock of white mice which had been inbred for many generations, and which showed in consequence a considerably diminished fertility, the white stock used by us gave no indications of extensive inbreeding; and yet in the experiments of von Guaita, as in our own, complete albinism is inherited in slightly more than the proportions demanded by Mendelian principles. The experiments of Cuénot also show a slight excess of albinos over expectation.

Inbreeding, then, does not affect the inheritance of complete albinism in crosses; whether it affects the character of the pigmentation of the hybrid individuals formed is an entirely different question, one which can be tested only by the use of albino individuals resulting from a cross between unrelated pure albino stocks. Such a cross should serve to counteract, at least in part, the effect of any previous inbreeding either in one or in both albino stocks. Our present opinion is that *purity* of the albino stock, rather than inbredness, is of consequence in determining the extent of reversion to the primitive gray pigmentation in the primary cross with mosaic individuals; but further experiments are needed to settle this point.

In the foregoing pages we have used such expressions as *impure albino* and *impure recessive*, expressions which seem incompatible with the hy-

pothesis of gametic purity, and which therefore require justification. Construed in the strictest sense, the doctrine of gametic purity is untenable. We cannot accept that interpretation of it which requires that the gametes formed by an individual be the *precise equivalents* in all respects of the respective gametes which united to form that individual. Mendel himself would not have assented to such an interpretation, for in the latter part of his original paper ('66) he clearly states the important principle that a composite character may undergo resolution into its elements in consequence of crossing. This allows a *part* of a complex character to pass into one gamete, while the remaining parts pass into another; in other words, it makes possible the formation of *mosaic gametes*, into whose composition the dominant and recessive characters may *both* enter in varying degree. All gametes which contain *any portion* of a dominant or of a recessive character associated with its opposite, are in reality *mosaic*; yet, if a gamete essentially recessive contains only *traces* of the dominant character, it may be convenient to recognize this fact in its designation, which we do by calling it an *impure* recessive.

In guinea-pigs the impurity of recessives tainted with the dominant character is commonly visible. Ordinary white guinea-pigs with pink eyes, though they invariably produce albinos when bred *inter se*, have a greater or less amount of sooty black pigment in the skin and hair of their ears, nose, and feet, showing the presence of a trace of the dominant character. Rarely is it possible to obtain an animal free from this visible taint, and even when obtained, we are informed by breeders, such individuals are likely to produce offspring with a certain amount of pigment on their ears or feet.

The so-called Himalayan rabbit is another illustration of a mosaic with a predominantly recessive (albino) character, in which the dominant (pigment-forming) character is localized precisely as in the impure albino guinea-pig, namely, at the extremities. Himalayan rabbits have brownish-black noses, ears, feet, and tails, being elsewhere snowy white and having pink eyes. They breed true *inter se*, yet, according to Darwin ('76, p. 114), may occasionally produce a silver-gray animal, in which the pigment is not restricted to the extremities. This condition must result from *liberation* of the dominant character from the strict localization which it has in ordinary individuals and which it must have also in the gametes that produce them.

In mice, on the other hand, impurity in recessive individuals is not visible, though doubtless sometimes present. So long as the breeder wishes only to obtain white mice, it makes no difference what the ances-

try of his breeding animals is. All albinos alike will produce only white offspring when bred to albinos. But if the breeder desires to cross his albinos with colored mice, the pedigree of the former is of consequence. Different albinos will, in crosses with the same pigmented stock, yield different results. This is shown both by Darbishire's experiments and by our own. In October, 1900, we began a breeding experiment in which a family of black-white mice was crossed with two different stocks of albino mice. All three stocks bred true among themselves; but, in crosses with the black-whites, one albino stock produced only gray or black offspring, whereas the other produced *no gray* offspring, but only black or fawn-colored ones, often extensively spotted with white. Manifestly the gametes formed by the two albino stocks, though all predominantly recessive, were not all alike. It is probable that some of them at least were impure, containing traces of a latent pigment-forming character. Such a latent character is apparently not liberated, in the case of mice, by a cross with a different stock of albinos; but this result can be secured, probably, by a cross with dominants. We infer this not only from the observed result in crosses between black-white and albino mice, but also from what has been observed to take place in guinea-pigs. On crossing a "dark-pointed" albino guinea-pig with a stock of red guinea-pigs which for a number of generations had bred true *inter se*, there were obtained offspring which in every instance were predominantly *black* in color, yet with a certain proportion of red hairs mixed with the black, which gave them a "brindle" or finely mottled black-and-red appearance. This result must be attributed to a liberation of the black-pigment-forming character either from its visible, strict localization in the albino parent, or from a possible latent and invisible occurrence in the red parent. We incline at present toward the former explanation, but the matter has not yet been fully tested. The complete disappearance of the albino character in this cross is noteworthy as being parallel to its behavior in the cross between black-white and white mice.

Darbishire's pink-eyed, fawn-white dancing mice were mosaics predominantly recessive, and might with some propriety be designated *impure* recessives, but they differed from impure guinea-pig recessives in that, when crossed with ordinary recessives, they did not produce pink-eyed animals like themselves, but rather animals which were in a majority of cases extensively pigmented. It seems more appropriate, therefore, to designate them *mosaics*.

"Dutch-marked" varieties of guinea-pigs, rabbits, and mice, and the

somewhat similarly marked Holstein and Hereford cattle, though they do not breed so true *inter se* as dark-pointed albino guinea-pigs or Himalayan rabbits or, perhaps, as pink-eyed dancing mice, nevertheless indicate a fairly precise localization of the pigment-forming and albino characters within mosaic germs.

If we adopt the Roux-Weismannian idea of the nature of the chromosomes, it is probable that particular chromosomes, or part chromosomes, in the mosaic germ, contain the dominant character, while the remaining chromosomes, or part chromosomes, contain the recessive character.

VI. Cross-breeding, Reversion, and the Doctrine of Gametic Purity.

Union with a recessive gamete usually, though not always, serves to break up this localization, allowing the dominant character to extend its influence throughout the entire body. This is the case, for example, in the cross between spotted and white mice in the experiments of Haacke, von Guaita, and in part of Darbishire, as well as in our own. It is possible to suppose in such cases either (1) that the resolving effect of the cross is restricted to the soma of the cross-bred, or (2) that it extends also to the germ-cells of the cross-bred. If the former hypothesis is correct, the cross-bred should form gametes $D\,R$ and R in equal numbers; if the latter, then only gametes D and R should be formed, and these in equal numbers. A simple test is afforded by the breeding *inter se* of hybrid mice produced by crossing pure mosaics with recessives. On the first hypothesis suggested, the offspring of the hybrids should consist, in at least one case out of four, of *spotted* mice formed by the union of two pure $D\,R$ gametes; on the second hypothesis *no spotted* mice should be produced, but only classes D, $D(R)$, and R, as in breeding together hybrids between wild gray mice and white mice. Von Guaita's experiments show the formation at the second filial generation of *nine spotted mice*, twenty-one uniformly gray or black mice, and fourteen white mice. The expectation on hypothesis (1) is 11 spotted : 22 gray or black : 11 white mice, which approximates closely the observed result; whereas on hypothesis (2) there should be *no* spotted mice, but only such as are pigmented all over or else are albinos. The result is conclusive in favor of hypothesis (1) — that a mosaic gamete, on uniting in fertilization with a recessive gamete, does not lose its own identity nor undergo resolution into its constituent parts.*

* Compare the results of Darbishire, as stated on p. 612, footnote.

Yet we must not fail to observe that a cross of the sort just described is not without its effects on the nature of the gametes; these do not retain their original character. For whereas the mosaic gametes of the original spotted parents produced, on union in pairs, invariably black-white offspring, the mosaic gametes formed by their hybrid offspring, when similarly combined, formed in von Guaita's experiments eight *gray*-white offspring, but only one *black*-white. Accordingly, though it seems certain that mosaic gametes may in crosses retain their mosaic character, the cross is nevertheless able to bring into activity characters latent in the parents, and to add these to the previous visible total of the mosaic, giving it thus a new character. In the original black-white stock, the mosaic consisted of the active characters, black and white, while the character yellow was latent, either in the mosaic gametes or in the recessive gametes with which they united when the cross was made. The cross brought at once into activity the latent character, yellow; and this combined with black to form the composite dominant character, *gray*, while white, though present in *both* gametes uniting, usually became for the time being altogether latent. But the gametes formed by the gray hybrid were not, as we should expect on the principle of strict gametic purity, *black*-white and white, but *gray*-white and white respectively. The character yellow, latent previous to the cross, having once become active remained so.

By this experiment we are put in possession of a principle of great importance, both theoretical and practical. It modifies essentially the Mendelian doctrine of gametic purity as commonly understood, yet without denying the soundness of that doctrine at core. It allows the breeder (as breeders habitually do) to reap substantial benefit from crosses, for in addition to permitting him to secure new combinations of the elementary characters visible in the parents crossed, it places at his disposal characters latent in the parents, and particularly facilitates the re-acquisition of lost characters.

The gray of hybrid mice obtained as in von Guaita's experiments is a composite character resulting from the combination of visible black with latent yellow. In Darbishire's experiments it results from the combination of visible yellow with latent black. In either case gray is obtained by synthesis (Bateson) of black and yellow. This view is supported by the observation of the reverse of this process, in crossing wild gray with white mice. In the second and later hybrid generations *black* pigmented as well as gray pigmented mice are obtained. These must result from a resolution of gray into its constituent elements, black and yellow, of which the latter then becomes latent.

It is not necessary to suppose, as Mendel apparently did, that the segregated elements of a composite character pass invariably into different gametes. There is reason to believe that yellow is frequently, if not always, latent in black mice, and black in yellow mice, though such an occurrence has not yet been conclusively demonstrated.

We would not, however, deny the possible correctness of Mendel's explanation in other cases. This should be indicated in breeding experiments by the simultaneous appearance in different individuals of the segregated elements of the composite character, and in particular numerical proportions. Each new sort should be incapable of producing the other, under either close or cross breeding. This is a subject well meriting more careful investigation.

VII. Summary.

1. Complete albinism, without a recorded exception, behaves as a recessive character in heredity.

2. Partial albinism is a mosaic condition in which the dominant pigment-forming character and the recessive albino character are visible in different parts of the same individual.

3. Pure mosaic individuals form only gametes which partake of their own mosaic nature. They and their gametes may be designated $D\,R$.

4. Hybrid mosaics result from the union of a mosaic gamete, $D\,R$, with a recessive gamete, R, as in a cross between a pure mosaic and a recessive individual. Such crosses are made when a race of spotted mice which breeds true is crossed with albinos.

5. Hybrid mosaic mice are usually more extensively pigmented than pure mosaics, frequently they are pigmented all over. When they are spotted with white, we may consider this the result of dominance of the mosaic gamete *as a unit* and may designate them accordingly, $D\,R\cdot(R)$. When they are pigmented all over, it is clear that the *dominant element* only of the mosaic gamete is visible in them. They should then be designated $D(R)\cdot(R)$.

6. The gametes formed by a hybrid mosaic are of two sorts, like those which united to produce it, namely, $D\,R$ and R. Accordingly when hybrid mosaic individuals breed together, they produce offspring of three different sorts, — pure mosaics, hybrid mosaics, and recessives. We should expect these three classes to be numerically as 1 : 2 : 1, and this is probably the case. When a hybrid mosaic is bred to a recessive, two sorts of offspring are produced, — hybrid mosaics and recessives. These classes should be of approximately equal size.

7. Albinism apparently complete may in reality conceal traces of the pigment-forming character either in an active or in a latent condition. Albinos thus constituted are in reality mosaics of the contrasted characters, but with the pigment-forming character (ordinarily dominant) occurring in a condition of partial or complete latency. When bred to other albinos they uniformly produce albinos, hence they may for convenience be distinguished as *impure* recessives. In guinea-pigs and rabbits the impurity of recessive individuals is, in certain cases at least, visible; in mice it apparently is not.

8. Cross-breeding is able to bring into activity latent characters or *latent elements* of a complex character. This is probably the true explanation of many cases of reversion. Conversely it is able to cause one or another element of a complex character to *become latent* and to *remain* so under close breeding. This principle probably explains how races of black or yellow mice may be obtained by crossing wild gray mice with albinos.

9. The Mendelian doctrine of gametic purity is fully substantiated by experiments in breeding mice, guinea-pigs, and rabbits, but with the important qualification stated under 8, a qualification which really enhances the practical utility of that doctrine in its every-day application by breeders.

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